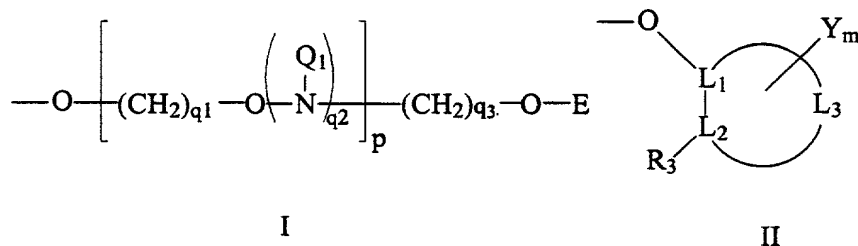


2'-C<sub>2</sub>H<sub>5</sub> ribonucleotides, 2'-CH=CH<sub>2</sub> ribonucleotides or 2'-C≡CH ribonucleotides. These are joined together in a contiguous sequence by phosphate, phosphorothioate, phosphorodithioate or boranophosphate linkages.

[0023] In a further preferred embodiment of the invention, each of the nucleotides of said further portion of nucleotides, independently, are selected to be 2'-fluoro nucleotides or nucleotides having a 2'-substituent

having the formula I or II:



wherein

E is C<sub>1</sub>-C<sub>10</sub> alkyl, N(Q<sub>1</sub>)(Q<sub>2</sub>) or N=C(Q<sub>1</sub>)(Q<sub>2</sub>);

[0024] each Q<sub>1</sub> and Q<sub>2</sub> is, independently, H, C<sub>1</sub>-C<sub>10</sub> alkyl, dialkylaminoalkyl, a nitrogen protecting group, a tethered or untethered conjugate group, a linker to a solid support, or Q<sub>1</sub> and Q<sub>2</sub>, together, are joined in a nitrogen protecting group or a ring structure that can include at least one additional heteroatom selected from N and O;

R<sub>3</sub> is OX, SX, or N(X)<sub>2</sub>;

each X is, independently, H, C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>1</sub>-C<sub>8</sub> haloalkyl, C(=NH)N(H)Z, C(=O)N(H)Z or OC(=O)N(H)Z;

Z is H or C<sub>1</sub>-C<sub>8</sub> alkyl;

[0025] L<sub>1</sub>, L<sub>2</sub> and L<sub>3</sub> comprise a ring system having from about 4 to about 7 carbon atoms or having from about 3 to about 6 carbon atoms and 1 or 2 hetero atoms wherein said hetero atoms are selected from oxygen, nitrogen and sulfur and wherein said ring system is aliphatic, unsaturated aliphatic, aromatic, or saturated or unsaturated heterocyclic;

[0026] Y is alkyl or haloalkyl having 1 to about 10 carbon atoms, alkenyl having 2 to about 10 carbon atoms, alkynyl having 2 to about 10 carbon atoms, aryl having 6 to about 14 carbon atoms, N(Q<sub>1</sub>)(Q<sub>2</sub>), O(Q<sub>1</sub>), halo, S(Q<sub>1</sub>), or CN;

each q<sub>1</sub> is, independently, from 2 to 10;

each q<sub>2</sub> is, independently, 0 or 1;

m is 0, 1 or 2;

p is from 1 to 10; and

q<sub>3</sub> is from 1 to 10 with the proviso that when p is 0, q<sub>3</sub> is greater than 1.

[0027] A more preferred group for use as the further portion of nucleotides are 2'-F ribonucleotides, 2'-O-(C<sub>1</sub>-C<sub>6</sub> alkyl) ribonucleotides, or 2'-O-(C<sub>1</sub>-C<sub>6</sub> substituted alkyl) ribonucleotides wherein the substitution is C<sub>1</sub>-C<sub>6</sub> ether, C<sub>1</sub>-C<sub>6</sub> thioether, amino, amino(C<sub>1</sub>-C<sub>6</sub> alkyl) or amino(C<sub>1</sub>-C<sub>6</sub> alkyl)<sub>2</sub>. These nucleotides are joined together in sequence by 3'-5' phosphodiester, 2'-5' phosphodiester, phosphorothioate, Sp phosphorothioate, Rp phosphorothioate, phosphorodithioate, 3'-deoxy-3'-amino phosphoroamidate, 3'-methylenephosphonate, methylene(methylimino), dimethylhydrazino, amide 3 (*i.e.*, (3')-CH<sub>2</sub>-NH-C(O)-(5')), amide 4 (*i.e.*, (3')-CH<sub>2</sub>-C(O)-NH-(5')) or boranophosphate linkages.

[0028] In one preferred embodiment of the invention, at least two of the nucleotides of the further portion of nucleotides are joined together in a contiguous sequence that is position 3' to the contiguous sequence of the first portion of nucleotides. In an additional preferred embodiment of the invention, at least two of the further portion of nucleotides are joined together in a continuous sequence that is position 5' to the continuous sequence of the first portion of nucleotides.

[0029] In a further preferred embodiment of the invention, at least two of the nucleotides of the further portion of nucleotides are joined together in a continuous sequence that is position 3' to the continuous sequence of the first portion of nucleotides and at least two of the further portion of nucleotides are joined together in a continuous sequence that is position 5' to the continuous sequence of the first portion of nucleotides.

[0030] A first preferred group of nucleotides for use as the first portion of nucleotides include 2'-SCH<sub>3</sub> ribonucleotides, 2'-NH<sub>2</sub> ribonucleotides, 2'-NH(C<sub>1</sub>-C<sub>2</sub> alkyl) ribonucleotides, 2'-N(C<sub>1</sub>-C<sub>2</sub> alkyl)<sub>2</sub> ribonucleotides, 2'=CH<sub>2</sub> ribonucleotides, 2'-CH<sub>3</sub> ribonucleotides, 2'-C<sub>2</sub>H<sub>5</sub> ribonucleotides, 2'-CH=CH<sub>2</sub> ribonucleotides and 2'-C≡CH ribonucleotides. A more preferred group include 2'-SCH<sub>3</sub> ribonucleotides, 2'-NH<sub>2</sub> ribonucleotides, 2'-NH(C<sub>1</sub>-C<sub>2</sub> alkyl) ribonucleotides, 2'-N(C<sub>1</sub>-C<sub>2</sub> alkyl)<sub>2</sub> ribonucleotides and 2'-CH<sub>3</sub> ribonucleotides. A further preferred group include 2'-SCH<sub>3</sub> ribonucleotides, 2'-NH<sub>2</sub> ribonucleotides and 2'-CH<sub>3</sub> ribonucleotides. Particularly preferred are 2'-SCH<sub>3</sub> ribonucleotides.

[0031] A further group of nucleotides that are preferred of use as the nucleotides of the first portion of the oligonucleotides of the inventions are 2'-CN arabino nucleotides, 2'-F arabino nucleotides, 2'-Cl arabino nucleotides, 2'-Br arabino nucleotides, 2'-N<sub>3</sub> arabino nucleotides, 2'-OH